Biomarkers and Mild Traumatic Brain Injury

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Impact of Mild TBI: Why We Should Care

- Reported as high as 20% of troops sustaining a mild TBI
- DOD and VA screening based on case definition of mTBI can results in underdiagnosis, overdiagnosis, and/or misdiagnosis
- Self report lacks specificity
- Overlap with PTSD Symptoms



The role of biomarkers in acute diagnosis; What about mTBI as chronic disease?

Brain

- Multiple cell types and distributions
- Cells with varying sensitivity to trauma
- Cells with differentially localized elements (axons, cell bodies)
- Blood-brain barrier limits access to vasculature

Heart

- Cellular homogeneity
- Uniform cell distribution
- Direct extracellular/ vascular access

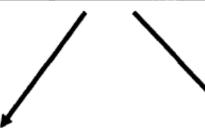
What is the ideal mTBI biomarker?

- A protein(s) released from injured neurons or glial cells
- Present in blood but not elevated in other conditions
- Rapid point of care platformoperator independent
- Sensitive to early trauma; low false negative rate
- Release patterns indicative of disease progression

Targeting Different Components of the Injury Cascade

Vascular occlusion & thrombosis

vWF Tissue Factor TAT III complex D-Dimer



Neuronal injury and stress response

NSE NGF

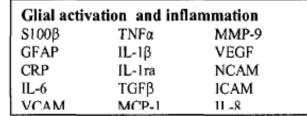
Neuropeptide Y HSP

CNTF CPK-BB

Nerve Growth Factor Secretagogin BNP RNA binding protein

Calbindin-D Neurotrophin 3 chimerin

c-tau





Apoptosis

Caspase 3

Cytochrome C

Myelin Breakdown

MBP

Ox-LDL

Proteolipid Protein

Neuroprostane

Fatty Acid Binding Protein

Return to combat guidelines

- Most symptoms resolve after 7-10 days following blast concussion
- Early underreporting and later overreporting of symptoms
- Objective measures of cognitive function lacking
- Prospective studies needed (civilian and military) to validate screening tools and biomarkers in collaborative fashion